

LOCHT et al -- Serial No.: 08/765,287

over Loosmore et al in view of Menozzi et al and Locht et al. The rejections are traversed for the reasons that follow.

The Examiner again takes the view that Loosmore et al discloses fusion proteins that comprise an amino acid sequence from Fha fused to an amino acid sequence from a protein distinct from Fha. Respectfully, it is believed that the Examiner's continued reliance on Loosmore results from some confusion over the distinction between a transcriptional fusion (wherein nucleoside sequences from two different origins are linked but do not result in a hybrid open reading frame encoding a fusion protein) and a translational fusion (wherein the gene fusion can be translated into a fusion protein encompassing two amino acid sequences from different origins).

In rejecting the claims as obvious, the Examiner directs attention to the gene fusions Fhap/TOX, Fahp/PRN and TOXp/Fha taught by Loosmore. Applicants point out, however, that these gene fusions do not code for "fusion proteins comprising an amino acid sequence from Fha fused to an amino acid sequence from a protein distinct from Fha". Rather, and as explained by Loosmore, these fusions were obtained "by fusing the promoters with the structural genes at the ATG start codon of the structural gene"

LOCHT et al -- Serial No.: 08/765,287

(column 4, lines 34-36). The next sentence of Loosmore specifies that "[s]uch fusions result in a native but autologous promoter, and a structural gene with its natural signal sequence" (emphasis added).¹

The fusions described by Loosmore thus comprise a nucleotide sequence from the Fha gene (i.e., the promoter sequence), and a nucleotide sequence from a gene heterologous thereto (i.e., the sequence encoding a structural gene such as TOX). However, as described unambiguously in Loosmore, the gene fusions taught do not encode a fusion protein comprising and amino acid sequence from Fha fused to an amino acid sequence from a protein distinct from Fha (as required by the claims).

It has been acknowledged that Menozzi et al teach that the Fha protein is able to interact with heparin. However, Applicants reiterate that an one skilled in the art reading this article and the application by Loosmore et al would not have arrived at the claimed invention, since the Loosmore et al reference is not relevant, for the reasons detailed above.

¹As pointed out previously, in the names of the gene fusions mentioned above, the letter "p" stands for "promoter". For example, Fhap/TOX designates a fusion between the Fha promoter and the TOX coding sequence.

LOCHT et al -- Serial No.: 08/765,287

The rejection of claims 34 , 35 and 37 over Loosmore et al in view of Menozzi et al and Locht et al is again traversed since, given the fundamental failings of the primary reference discussed above, there is nothing in Locht et al that would have suggested making fusion proteins with an Fha moiety.

Reconsideration is requested.

Claims 40 and 41 stand rejected under 35 USC as allegedly being anticipated by Relman et al. The rejection is traversed.

Relman et al describes the purification of large amounts of Fha fragments. To that end, the FhaB open reading frame was divided into seven fragments that were separately cloned into the expression vector pEX34, which comprises a promoter and a sequence encoding the N-terminal 98 amino acids of the MS2 RNA polymerase. This is explained, for example, at column 9, lines 45 to 59 of Relman.

The Examiner contends that Relman et al teaches fusion proteins having a N-terminal moiety consisting of an Fha N-terminal fragment (the Examiner directs attention to column 2, lines 30-35, and claims 8-10). However, the cited paragraph of column 2 merely describes the Fha ORF, specifying that it comprises a N-terminal fragment of 230

LOCHT et al -- Serial No.: 08/765,287

kDa, and the indicated claims recite nucleic acids encoding the amino-terminal 313 kDa of the FHA protein (claims 8 and 9), and an expression construct comprising this nucleic acid operably linked to other nucleic acids comprising transcription initiation and termination regions (claim 10). None of the claims to which the Examiner refers describes or would have suggested the construction of a fusion protein comprising a N-terminal moiety originating from FHA. Applicants submit that the fusion proteins described by Relman et al all comprise a N-terminal moiety from MS2 and a C-terminal moiety corresponding to a fragment of FHA. Although one fusion comprises the N-terminal extremity of FHA, this fragment is still in the C-terminal portion of the corresponding fusion protein.

Enclosed is an article by Domenighini, Relman and others, describing the same fusion proteins as those mentioned in USP 6,036,960. In this article, the authors refer to a publication by Strebel et al (1986), apparently as describing pEx34 (see page 794, second paragraph of left column of Domenighini et al). The article by Strebel et al is also enclosed. It will be noted that Strebel et al does not recite exactly a "pEx34" plasmid, but that it describes several expression vectors for the construction of fusion

LOCHT et al -- Serial No.: 08/765,287

proteins, designated "pPLc24", "pEx30", "pEx31" and "pE34". All of these vectors are designed to construct fusion proteins in which the N-terminal moiety consists of 98 N-terminal amino acids of the MS2 polymerase. This appears clearly in the last paragraph of page 984 (pE34 vector) and Figure 1 (pEx30 and pEx31).

An article by Nicosia et al (1987) is enclosed that explicitly mentions the pEx34 vector. In this article, pEx34 is defined as a derivative of pEx29, together with pEx31 (see first paragraph of Materials and Methods). To describe these vectors, Nicosia et al refers to the Strebel reference described above and to another article by Klinkert et al (see the last paragraph of page 964 of Nicosia et al for this reference). Klinkert et al (1985, copy of which is also enclosed) describes the pEx29 expression vector and it appears clear, from paragraph 2 of page 230 and from Figure 2, that the fusion proteins obtained using this vector comprise a fragment of the MS2 protein as their N-terminus.

In view of the above, it will be clear that the fusion proteins described in the cited Relman patent have a N-terminal moiety from MS2 and a C-terminal moiety from Pha. Hence, the Examiner's assertions to the contrary, the

LOCHT et al -- Serial No.: 08/765,287

citation does not anticipate the subject matter of the
rejected claims. Reconsideration is requested.

This application is submitted to be in condition for
allowance and a Notice to that effect is requested.

Respectfully submitted,

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